Conversion of mouse epiblast stem cells to an earlier pluripotency state by small molecules.

Journal: J Biol Chem

Publication Year: 2010

Authors: Hongyan Zhou, Wenlin Li, Saiyong Zhu, Jin Young Joo, Jeong Tae Do, Wen Xiong, Jeong Beom Kim, Kang Zhang, Hans R Scholer, Sheng Ding

PubMed link: 20705612

Funding Grants: Derivation of New ICM-stage hESCs

Public Summary:
Epiblast stem cells (EpiSCs) are pluripotent cells derived from post-implantation late epiblasts in vitro. EpiSCs are incapable of contributing to chimerism, indicating that EpiSCs are less pluripotent and represent a later developmental pluripotency state compared with inner cell mass stage murine embryonic stem cells (mESCs). Using a chemical approach, we found that blockage of the TGFbeta pathway or inhibition of histone demethylase LSD1 with small molecule inhibitors induced dramatic morphological changes in EpiSCs toward mESC phenotypes with simultaneous activation of inner cell mass-specific gene expression. However, full conversion of EpiSCs to the mESC-like state with chimerism competence could be readily generated only with the combination of LSD1, ALK5, MEK, FGFR, and GSK3 inhibitors. Our results demonstrate that appropriate synergy of epigenetic and signaling modulations could convert cells at the later developmental pluripotency state to the earlier mESC-like pluripotency state, providing new insights into pluripotency regulation.

Scientific Abstract:
Epiblast stem cells (EpiSCs) are pluripotent cells derived from post-implantation late epiblasts in vitro. EpiSCs are incapable of contributing to chimerism, indicating that EpiSCs are less pluripotent and represent a later developmental pluripotency state compared with inner cell mass stage murine embryonic stem cells (mESCs). Using a chemical approach, we found that blockage of the TGFbeta pathway or inhibition of histone demethylase LSD1 with small molecule inhibitors induced dramatic morphological changes in EpiSCs toward mESC phenotypes with simultaneous activation of inner cell mass-specific gene expression. However, full conversion of EpiSCs to the mESC-like state with chimerism competence could be readily generated only with the combination of LSD1, ALK5, MEK, FGFR, and GSK3 inhibitors. Our results demonstrate that appropriate synergy of epigenetic and signaling modulations could convert cells at the later developmental pluripotency state to the earlier mESC-like pluripotency state, providing new insights into pluripotency regulation.